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EFFECTS OF PROLONGED CONTINUOUS EXPOSURE OF HUMAN SKIN TO WATER: A REASSESSMENT

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Continuous exposure of human skin to water in small plastic cups for periods of 72 and 144 hr produced a mild, transient dermatitis in half the sites tested. The degree of dermatitis was only slightly greater at 144 than at 72 hr, and was unrelated to the pH of the water samples. Comparison of soap-pretreated to non-pretreated skin areas showed a significant tendency for the more severe dermatitis to be present on the non-pretreated skin areas at higher pH's. There was virtually no coating of hairs with waxy yellowish material (clumps of bacteria), and no lesion was produced that resembled warm-water-immersion injuries.

Excessive exposures of human skin to water can produce or aggravate a variety of pathologic conditions, including chronic hand eczema, asteatosis, primary irritant dermatitis, eruptions such as ring dermatitis [1], and several types of immersion foot [2,3]. In some instances it is possible to incriminate detergents, industrial chemicals, and microorganisms as the inciting agents, but in others it appears that water itself is the primary offender. The role of water in such injuries which include warm-water dermatitis, is poorly understood.

Willis [4] attempted to explore the role of water in the pathogenesis of such dermatoses by developing a model of water-immersion injury in human subjects. "Striking inflammation" was reported to occur after 72 to 144 hr of continuous exposure of the skin of the back to water in small plastic cups. Contrary to expectations, neither the induction nor the intensity of responses appeared to be dependent on increases in skin surface pH or the size of bacterial populations.

We questioned the absence of pH-related effects and decided to further investigate the role of pH using the techniques developed by Willis. Pilot studies showed no dermatitis when water-filled cups were worn continuously on the forearm, thorax, or lower leg for 120 hr. Since these studies differed from those of Willis both in body site and in lack of bathing with Ivory soap, we adopted the methods originally described but with the addition of a balanced experimental design and double-blind grading of dermatitis. Although we used identical cups, buffer systems, body sites, and types of subjects, our results differed substantially from those reported previously by Willis.

MATERIALS AND METHODS

The 5-ml-capacity clear Plexiglass cups developed by Willis were used; however, the method of attaching them to the backs of the volunteers differed. In this study, each cup was glued to an A-D double-sided adhesive disc with sterile viscous isoamyl 2-cyanoacrylate. A thin rim of cyanoacrylate was applied to the underside of the disc immediately under the cup lip, and the cup was affixed to the back and secured with Blenderm plastic tape. Erythema and edema from the tape, which exceeded the reaction to the adhesive disc, eventually led to the elimination of both tape and discs from the experiment. The cups were then affixed directly to the skin using only the cyanoacrylate glue. A similar system has been used successfully in rats [5].

Water samples. Water samples consisted of sterile water for injection (no preservative, pH 6.55) and sterile buffered solutions of 0.1 M *N*-2-hydroxyethyl-piperazine-*N*-2-ethanesulfonic acid (HEPES) at pH 3.5 and pH 7.5.

Methods of testing. The subjects were 14 healthy, consenting, young white men. The right or left sides of their backs, randomly chosen, were washed once a day with Ivory soap for 14 days prior to the experiment. The subjects also showered once a day during this period using their preferred brand of soap (Dial, Safeguard, Dove).

After the 14-day preparation of the subjects, 6 water cups were affixed to the back of each subject (3 on each side in the upper, middle, and lower back). Four milliliters of each solution was placed in the cups in a randomized and balanced fashion so that each test site was exposed with equal frequency to water at each of the three pH's. The water samples were placed in inverse order on the opposite side of the back.

Water was left in continuous contact with the skin for 72 hr, after which the cups were removed and the dermatitis graded. The cups were replaced after 1 hr, filled with fresh solution, and worn for 72 hr more.

Evaluation of responses. All clinical responses to water exposure were evaluated "blind" by a single observer (AMA) using three independent grading systems: (1) Willis's system; (2) rank ordering of sites based on a global assessment of intensity of dermatitis; and (3) the scale shown in Table I.

RESULTS

In the periods immediately after removal of the water-filled cups at 72 and 144 hr, virtually no dermatitis was visible due to opacity of the horny layer. About 1 hr later, some sites showed varying degrees of inflammation, none of which was strik-

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TABLE 1. *Criteria for grading dermatitis by individual clinical sign*

Score	Erythema	Edema	Vesicles	Pustules	Perifollicular papules
0	None	None	None	None	None
1	Patchy	< 1 mm	<4 pinpoint	1–3	"Stippled appearance"
2	Confluent and non-intense	1–2 mm	>4 pinpoint	3–10	"Gooseflesh appearance"
3	Confluent and intense	>2 mm	Larger than pinpoint	10	Nonfollicular papules

ing. On average, lesions were slightly more severe at 144 than at 72 hr, but this did not pertain to every subject. All signs of skin damage were gone within 24 hr after final removal of the water-filled cups.

Table II shows the results using Willis's grading system on the soap-washed side of the back after 144 hr of exposure to water. Overall, half the water-exposed sites in our study showed no response, and only 2 of 42 sites (5%) showed a reaction intensity of 2+ or greater. Identical results were obtained on the side of the back not treated with soap. In contrast, all 90 sites in Willis's study were reported to have reaction intensities of 2+ or greater. Willis's data showed a statistically significant trend towards increasing severity of dermatitis with increasing pH of the water samples (linear trend in proportions $\chi^2 = 4.7$, $p < 0.05$). Our data, however, showed no such trend.

In Willis's grading system a score of zero was assigned in cases where there was edema or other signs of inflammation but no erythema. We therefore developed alternative grading systems (see *Materials and Methods*) to extract the maximum amount of information from the experiment. The results obtained when the severity of each of five signs of inflammation was recorded separately showed no pH-related effects. Slight, nonconfluent erythema and minimal edema were the principal signs observed.

Since the amount of dermatitis was so slight, neither of the defined grading systems mentioned above could distinguish between the slight variations in erythema and edema. Evaluation by global assessment (a form of rank ordering) provided a better basis for comparison because it forced the grader to make fine distinctions. The scores assigned by global assessment were used to evaluate the effects of both pH and soap treatment. There was a tendency for water at the more acid pH's to produce a greater dermatitis on the soap-washed side of the back. An analysis of variance for ranked data (Friedman's test) was not statistically significant ($\chi^2 = 5.6$, $p < 0.05$). On the non-pretreated side, there was a tendency for greater dermatitis to be noted with water at the more alkaline pH's, but again the results were not statistically significant. The global assessment evaluation agrees with the Willis system and the individual clinical sign evaluation (Tab. I), i.e., there was no statistically significant pH effect.

When the global assessment scores were used to compare the soap-pretreated sites to the non-pretreated sites at each pH, a more direct examination of soap-related effects can be seen (Tab. III). Since each subject had 2 cups at each pH, one on soap-pretreated skin and the other on non-pretreated skin, the site blindly graded as having the greatest dermatitis was recorded in the appropriate column (Tab. III).

If soap pretreatment had no effect, then on 7 subjects the soap side would have scored as the most severe dermatitis and in the other 7 the non-pretreated side would have scored as most severe at each of the 3 pH's. This comparison (Tab. III) revealed that more severe dermatitis was produced at the more alkaline pH's on the non-pre-

TABLE II. *Intensity of skin reactions to hydration according to Willis's grading system*

Test site pH	Reaction intensity	Present study[a]		Willis's study	
		No. sites	%	No. sites	%
3.5	0	5	36	0	0
	1	8	57	0	0
	2	1	7	11	37
	3	0	0	19	63
	4	0	0	0	0
		14	100	30	100
5.5	0	8	57	0	0
	1	6	43	0	0
	2	0	0	5	17
	3	0	0	25	83
	4	0	0	0	0
		14	100	30	100
7.5	0	8	57	0	0
	1	5	36	0	0
	2	0	0	4	13
	3	1	7	20	67
	4	0	0	6	20
		14	100	30	100

[a] Soap-pretreated sides only

TABLE III. *Influence of soap pretreatment in relation to pH of water samples*[a]

pH	Greater dermatitis produced on soap-pretreated side	Greater dermatitis produced on non-pretreated side
3.5	9	5
5.5	5	9
7.5[b]	1	12

[a] Observations made after 144 hr of water exposure, by global assessment of 14 subjects

[b] One observation incorrectly recorded, thus only 13 observations

treated side. This trend was statistically significant (linear trend in proportions $\chi^2 = 9.3$, $p < 0.01$).

Hairs were thickly coated with waxy yellowish material at 1 of the 6 sites in only 2 of the 14 subjects.

DISCUSSION

In this study, a mild, transient dermatitis was produced by exposing the skin of the back to water for 6 days. These results differ substantially from those described by Willis [4], who reported that "striking inflammation" occurred under virtually identical conditions of water immersion. No subject developed skin lesions similar to the warm-water-immersion dermatoses with which we are familiar [2,6] and, therefore, the water-cup technique does not appear to be useful in producing a model system for water-immersion injury.

The marked difference in results between the present study and that reported by Willis [4] is difficult to explain since both were conducted under apparently similar conditions. There appeared to be no systematic differences in experimental technique other than the manner in which the cups were applied to the skin. Whether the method of cup affixation was responsible for the dermatitis observed by Willis can only be answered by further experimentation, but in any event water immersion alone cannot be incriminated. Since Willis's grading system permitted sharp, unequivocal cut points to be made between various degrees of inflammation, it is unlikely that the reported differences are merely an artifact due to semantic confusion or observer variation.

Our principal focus of interest was on possible pH-related effects, especially since Willis's data suggested a tendency for immersion dermatitis to be more severe at higher pH's. Our data showed no apparent relationship between pH and severity of dermatitis on either the soap-pretreated or the non-pretreated sides of the back, and therefore we are in agreement with Willis's impression that neither the induction nor the intensity of responses was dependent on increases in skin surface pH.

The comparison between soap-pretreated and non-pretreated sides of the back suggested that simple soap-and-water washing may not be an innocuous procedure when looking for pH-related effects of water immersion. The observed tendency for the more severe dermatitis to appear on the non-pretreated areas at higher pH's suggests that "alkaline hardening" by soap pretreatment may have diminished our ability to detect pH-related events [7]. Therefore, it may not be safe to assume that use of a mild, nonantibacterial soap prior to an experiment such as this will have no appreciable effect on the outcome. However, this point cannot be considered established in the absence of confirmatory evidence.

We found coating of hairs with waxy yellowish material (clumps of bacteria) to be rare, whereas Willis [4] observed these clumps of gram-positive, rod-shaped bacteria resembling *Propionibacterium acnes* in nearly every water-immersed site. The reason for this difference is not known; however, there may be a correlation between the presence of bacteria and the induction and intensity of dermatitis despite Willis's evidence to the contrary. This could provide a plausible explanation for the marked differences in findings between our study and his.

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